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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/746,581	12/21/2000	Therese Jourdier	00,1287	1597

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/746,581	JOURDIER ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *6 and 7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Currently, claims 1-10 are pending in the application.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 18, 2004 has been entered.

3. In the prior action, mailed on April 20, 2004, claims 1-5, and 8-10 were rejected, and claims 6 and 7 were withdrawn as to non-elected inventions. In the Response filed on June 18, 2004, the Applicant amended claim 1. Currently, claims 1-5, and 8-10 are under consideration.

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date to PCT Application PCT/FR99/01554 under 35 U.S.C. 120 as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). While the Applicant has amended the specification to include reference to an earlier filed application, this reference was not made in accordance with 37 CFR 1.78 because the amendment was not accompanied by a grantable petition as described below.

The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. This reference must be submitted during the pendency of the later-filed application. **If the later-filed application is an application filed under 35 U.S.C. 111(a), this reference must also be submitted within the later of four months from the actual filing date of the later-filed application or sixteen months from the filing date of the prior-filed application.** If the later-filed application is a nonprovisional application which entered the national stage from an international application after compliance with 35 U.S.C. 371, this reference must also be submitted within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371 (b) or (f) in the later-filed international application or sixteen months from the filing date of the prior-filed application. **These time periods are not extendable. Except as provided in paragraph (a)(3) of this section, the failure to timely submit the reference required by 35 U.S.C. 120 and paragraph (a)(2)(i) of this section is considered a waiver of any benefit under 35 U.S.C. 120, 121, or 365(c) to such prior-filed application.**

A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. **(Prior Rejection- Maintained)** Claims 1- 3, 5, and 8-10 were rejected under 35 U.S.C. 103(a) as being unpatentable over Thibodeau et al. (C R Acad Sci, Paris 313: 389-94- of record in the IDS of March 2001), in view of the teachings of Lowell et al. (the Lowell patent, U.S. Patent 5,985,284) and Heiber et al. (U.S. Patent 5,516,523). The claims have been amended so that they read on a method of producing a local and systemic immune response in a buccal mucous membrane, saliva, and draining lymph nodes to said mucous membrane through the administration to the floor of a primates mouth an immunogen against a pathogen with a gateway into the buccal mucous membrane. The Applicant identifies HIV as such a pathogen in claim 5. The claim additionally states that such an administration induces a local and systemic IgA and IgA producing B-cell response.

With respect to the amendment of the induction of a systemic immune response, it is noted first that the Kozlowski reference indicates that serum IgG was elicited through each of the three mucosal immunization routes described therein. From these teachings, those in the art would have had a reasonable expectation that mucosal immunization would generally result in such a response. Additionally, as indicated in the prior actions, the art suggests the use of

sublingual immunization to induce mucosal responses. Because the art suggests this route or administration, the Applicant's (asserted) discovery that this route of administration would also lead to a systemic response is merely recognition of a latent property in a known method of inducing an immune response. Such does not render a known invention patentable. See e.g., MPEP 2145, section II. Thus, the addition of this limitation does not overcome the rejection.

The Applicant provides three arguments in traversal. The first argument is that the cited references do not alone, or in combination teach or suggest the elements of the claimed methods. The second argument relates to the teachings of a reference (Kozlowski et al) relied on be the Office to show that local mucosal immunization is known to lead to immune responses at distant mucosal sites. Finally, the Applicant again argues that there is no basis for accepting that the teachings of the Thibodeau would be applicable to primates. These arguments are not found persuasive.

With respect to the first argument, the Applicant asserts that none of the references alone teaches or suggests the administration of an immunogen to the floor of a primate's mouth. In particular, the Applicant asserts that that Heiber reference does not suggest the administration of an immunogen through sublingual routes. The Applicant argues that because the reference is directed to the delivery of therapeutics, not of immunogens, there would have been no motivation to administer an immunogen through this mucosal membrane. This argument is not found persuasive because the Heiber reference is not being used alone with the teachings of Thibodeau, but is used in combination with Lowell. Lowell explicitly indicates that the sublingual mucosa is a suitable surface for the induction of a mucosal immune response. The additional teachings in Heiber merely demonstrate that those in the art would have known that

among the oral mucosa known in the art for immunogen administration, the sublingual membrane is also known to be more permeable to therapeutic substances in general. Because immunogenic compositions are therapeutic in nature, it would therefore have been apparent to those in the art that the teachings of Heiber would also apply to the administration of an immunogen. The Applicant's first argument in traversal is therefore not found persuasive.

The Applicant next takes issue with the reference to the Kozlowski et al reference, indicating that the teachings of the reference 1) are directed to a different method that those of the present claims, and 2) that the teachings in the reference contain "mixed teachings and does not provide the ordinary artisan with a reasonable expectation that administration to the floor of the mouth would result in an immune response in the buccal membrane." These arguments are also not found persuasive. With respect to the first argument, the fact that the teachings of Kozlowski are primarily concerned with mucosal administration at other sites than the sublingual mucosa does not make the references more general teachings inapplicable to what one of ordinary skill in the art would have known regarding the claimed invention.

The second argument with respect to the Kozlowski reference is that the reference provides 'mixed teachings" regarding the ability of a local immunization to induce responses at distant mucosal sites. However, the teachings referred to are based on the inability of vaginal immunizations to induce immune responses in the rectum. This is not found relevant to the present claims as these teachings are limited to vaginal immunization; an immunization route the reference indicates has peculiar properties from other mucosal surfaces. See, page 1387 (teaching that the organization of the vaginal mucosa lacks organized mucosal tissue). The reference nowhere teaches that this property is general to the mucosal tissues, or indicates that other

mucosal immunizations are similarly unable to generate reactions at distant sites. Thus, the teachings of Kozlowski are not, as suggested by the Applicant, mixed with reference to the ability of mucosal immunization to induce distant reactions in general. Rather, the reference supports the general teachings, but indicates that the peculiarities of a specific mucosal surface may indicate why the expected result was not seen in a specific case.

The final argument is that the Examiner has not met the burden of establishing that the teachings in the art relating to the administration of results in rabbits could be extended to primates. The Applicant contends that it would not have been obvious to those in the art that a mucosal response could be induced in a primate simply because it has been done in rabbits. However, the Examiner notes that the teachings in the art in general indicate that those in the art would have expected sublingual administration of an immunogen to induce an immune response. In addition to the teachings in Lowell, several additional references indicating as much were cited in the action mailed on April 20, 2004. Thus, the Examiner has provided sufficient evidence that those in the art would have expected that sublingual administration to induce an immune response in primates. The Applicant has presented no evidence that those in the art would not have expected sublingual administration in a primate to result in an immune response. As the Applicant has provided no more than an unsupported assertion to the contrary, the traversal is not found persuasive.

7. **(Prior Rejection- Maintained)** Claims 1-3, 5, and 8-10 were rejected under 35 U.S.C. 103(a) as being unpatentable over Thibodeau, Heiber, and Lowell as applied above, and further in view of Mathiowitz et al. (U.S. Patent 6,235,313) and Irwin et al. (WO 96/20731- of

record in the March 2001 IDS). No additional arguments, over those presented above, have been presented. The rejection is therefore maintained for the reasons above, and the reasons of record.

8. **(Prior Rejection- Maintained)** Claims 1-5, and 8-10 were rejected under 35 U.S.C. 103(a) as being unpatentable over Thibodeau, Heiber, and Lowell as applied above, and further in view of either Lowell et al. (J Infect Dis 175: 292-301), or Gandhi et al. (Adv Drug Deliv Rev, 13: 43-74). No additional arguments, over those presented above, have been presented. The rejection is therefore maintained for the reasons above, and the reasons of record.

9. **(Prior Rejection- Maintained)** Claims 1-5, and 8-10 were rejected under 35 U.S.C. 103(a) as being unpatentable over Hinkula et al. (Vaccine 15: 874-78- of record in the IDS of March 2001) in view of Irwin and Beckenkamp (HNO 33:196-203), and further in light of the teachings of Kozlowski et al. (Infect Immun 65(4): 1387-94), and Gorse et al. (Clin Diag Lab Immunol 3(6): 769-73). The claims have been amended as described above. However, this amendment is not deemed to avoid the rejection because the added limitation is merely recognition of a latent property in a known method as was described above. As no additional arguments have been presented over those set forth in the arguments of June 18, 2004 or addressed with reference to the rejections above, the rejection is maintained for the reasons above, and the reasons of record.

10. **(Prior Rejection- Maintained)** Claims 1-5, and 8-10 were rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over

Becker et al. (U.S. Patent 6,379,675) in view of Gorse and Beckenkamp. The claims have been described above. The Applicant traverses this rejection on the grounds that 1) the teaching of Hinkula is limited to mice and that those in the art would have had no reasonable expectation of success in using the indicated method with primates, and 2) that the Beckenkamp reference teaches away from the claimed method. Each of these arguments substantially restates the Applicant's arguments presented above in reference to, respectively, the rejections over Thibodeau, Heiber, and the Lowell, and the rejection over Hinkula, Irwin, Beckenkamp, Kozlowski and Gorse. These arguments are not found persuasive for the same reasons as indicated with respect to the rejections above. The rejection is therefore maintained, and extended to new claim 10.

11. **(New Rejection)** Claims 1-5, 8, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weiner et al. (WO 96/18390) in view of Heiber. The claims have been described above. It is noted that the claims are drawn to the administration of an immunogen. The Applicant argues in the Response filed on September 20, 2004 that an immunogen "is a compound able to induce a specific immune response," whereas an antigen "is simply a compound that is able to react with an antibody." Thus, the claims are drawn to the administration of any compound that is able to induce a specific immune response, particularly against an HIV antigen.

The Weiner reference suggests such a composition. This reference teaches the sublingual administration of a DNA encoding a protein such that a mucosal immune response is raised against that immunogen. Abstract. Because such DNAs appear to fall within the definition of

"immunogen" as described by the Applicant, the compositions of Weiner meet this limitation of the claimed invention. Among the antigens suggested are anti-HIV antigens. Pages 13-15. Additionally, the reference teaches the inclusion in the compositions of compounds to increase the uptake of the polynucleotides. Pages 24-25. From these teachings, it would also have been obvious to those in the art to include a penetration enhancer such as those described in Heiber. The Weiner reference also teaches that the administration of such compositions to induce an immune response leads to a "broad based," and includes humoral and mucosal immune responses. These teachings therefore render obvious the claimed invention.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

12/13/04